

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Canceled)
2. (Previously Presented) A composition comprising the compound of claim 59 and a pharmaceutically acceptable carrier.
- 3-13. (Canceled)
14. (Original) The composition of claim 2, further comprising at least one therapeutic agent.
15. (Original) The composition of claim 14, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H₂ antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.
16. (Original) The composition of claim 15, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen or naproxen.
- 17-27. (Canceled)
28. (Previously Presented) A composition comprising at least one compound of claim 59 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.
29. (Original) The composition of claim 28, further comprising a pharmaceutically acceptable carrier.
30. (Original) The composition of claim 28, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

31. (Original) The composition of claim 30, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione, or S-nitroso-cysteinyl-glycine.

32. (Previously Presented) The composition of claim 30, wherein the S-nitrosothiol is:

- (i) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{SNO}$;
- (ii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{R}_e$; or
- (iii) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_m-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, a carboxamido, an alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, an arylsulfonyloxy, a urea, a nitro, -T-Q-, or $-(\text{C}(\text{R}_g)(\text{R}_h))_k\text{-T-Q}$ or R_e and R_f taken together are an oxo, a thial, a heterocyclic ring, a cycloalkyl group, an oxime, a hydrazone or a bridged cycloalkyl group; Q is -NO or -NO₂; and T is independently a covalent bond, a carbonyl, an oxygen, -S(O)_o- or -N(R_a)R_i-, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, -CH₂-C(T-Q)(R_g)(R_h), or $-(\text{N}_2\text{O}_2)^-\bullet\text{M}^+$, wherein M⁺ is an organic or inorganic cation; with the proviso that when R_i is -CH₂-C(T-Q)(R_g)(R_h) or $-(\text{N}_2\text{O}_2)^-\bullet\text{M}^+$; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group; and R_g and R_h at each occurrence are independently R_e.

33. (Original) The composition of claim 28, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, nitrosated L-homoarginine, nitrosylated L-homoarginine), citrulline, ornithine, glutamine, lysine, an arginase inhibitor or a nitric oxide mediator.

34. (Original) The composition of claim 28, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

- (i) a compound that comprises at least one ON-O- or ON-N- group;
- (ii) a compound that comprises at least one O₂N-O-, O₂N-N- or O₂N-S- or group;
- (iii) a N-oxo-N-nitrosoamine having the formula: R^{1''}R^{2''}N-N(O-M⁺)-NO, wherein R^{1''} and R^{2''} are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M⁺ is an organic or inorganic cation.

35. (Original) The composition of claim 34, wherein the compound comprising at least one ON-O- or ON-N- group is an ON-O-polypeptide, an ON-N-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, an ON-O-heterocyclic compound or an ON-N-heterocyclic compound.

36. (Previously Presented) The composition of claim 34, wherein the compound comprising at least one O₂N-O-, O₂N-N- or O₂N-S- group is an O₂N-O-polypeptide, an O₂N-N-polypeptide, an O₂N-S-polypeptide, an O₂N-O-amino acid, O₂N-N-amino acid, O₂N-S-amino acid, an O₂N-O-sugar, an O₂N-N-sugar, O₂N-S-sugar, an O₂N-O-oligonucleotide, an O₂N-N-oligonucleotide, an O₂N-S-oligonucleotide, ; a straight or branched, saturated or unsaturated,

aliphatic or aromatic, substituted or unsubstituted O₂N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-S-hydrocarbon, an O₂N-O-heterocyclic compound, an O₂N-N-heterocyclic compound or an O₂N-S-heterocyclic compound.

37. (Original) The composition of claim 28, further comprising at least one therapeutic agent.

38. (Original) The composition of claim 37, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a HMG CoA inhibitor, a H₂ antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

39. (Original) The composition of claim 38, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen or naproxen.

40-54. (Canceled)

55. (Currently Amended) A compound selected from the group consisting of:
4-(5-((2,2-difluoro-3-hydroxypropoxy)methyl)-3-phenylisoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;
4-(3-phenyl-5-(2,2,3,3-tetrafluoro-4-hydroxy)methyl)isoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;
4-(5-((2,2,3,3,4,4-hexafluoro-5-hydroxypentyloxy)methyl)-3-phenylisoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;
4-(5-((2-((2-hydroxyethyl)sulfonyl)ethoxy)methyl)-3-phenylisoxazol-4-yl) benzenesulfonamide or a pharmaceutically acceptable salt thereof;
4-(5-(3-nitrooxy)propoxy)methyl)-3-phenylisoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;

4-(5-(2-nitrooxy)ethoxy)methyl-3-phenylisoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;

~~4-(5-((2,2-difluoro-3-(nitrooxy)propoxy)methyl)-3-phenylisoxazol-4-yl)benzenesulfoamide~~ 4-(5-((2,2-difluoro-3-(nitrooxy)propoxy)methyl)-3-phenylisoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;

4-(3-phenyl-5-{[2,2,3,3-tetrafluoro-4-(nitrooxy)butoxy]methyl}isoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof;

4-(5-((2,2,3,3,4,4-hexafluoro-5-(nitrooxy)pentyl)oxy)methyl)-3-phenylisoxazol-4-yl)benzenesulfonamide or a pharmaceutically acceptable salt thereof; and

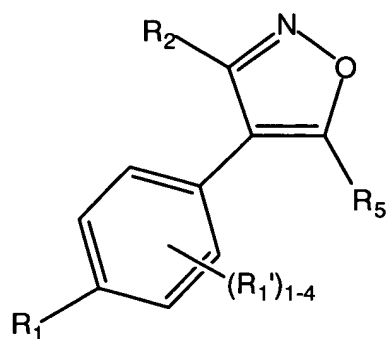
4-(5-((2-(nitrooxy)ethyl)sulfonyl)ethoxy)methyl)-3-phenylisoxazol-4-yl) benzenesulfonamide or a pharmaceutically acceptable salt thereof.

56. (Original) A composition comprising at least one compound of claim 55 and a pharmaceutically acceptable carrier.

57. (Original) The composition of claim 56, further comprising (i) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

58. (Cancelled)

59. (Currently Amended) A compound of Formula (III) or a pharmaceutically acceptable salt thereof:



III

wherein:

R₅ is:

- (a) $-(C(R_4)(R'_4))_k-Y-(C(R_4)(R'_4))_k-B-(C(R_4)(R'_4))_k-O-V$;
- (b) $-(C(R_4)(R'_4))_k-Y-(C(R_4)(R_4))_k-D-(C(R_4)(R'_4))_k-O-V$;
- (c) $-C(Z)-(C(R_4)(R'_4))_k-Y-(C(R_4)(R'_4))_k-O-V$;
- (d) $-(C(R_4)(R'_4))_k-Y-W-Q-(C(R_4)(R'_4))_k-O-V$;
- (e) $-C(Z)-W-Q-(C(R_4)(R'_4))_k-O-V$;
- (f) $-(C(R_4)(R'_4))_p-E-N(R_i)-O-W-Q-(C(R_4)(R'_4))_k-O-V$;
- (g) $-(C(R_4)(R'_4))_p-E-N(R_i)-O-(C(R_4)(R'_4))_k-O-V$;
- (h) $-(C(R_4)(R'_4))_p-N(R_i)-O-(C(R_4)(R'_4))_k-O-V$;
- (i) $-(C(R_4)(R'_4))_p-O-N(R_i)-(C(R_4)(R'_4))_k-O-V$;
- (j) $-(C(R_4)(R'_4))_p-O-N(R_i)-E-(C(R_4)(R'_4))_k-O-V$; or
- (k) $-(C(R_4)(R'_4))_p-O-N(R_i)-E-W-Q-(C(R_4)(R'_4))_k-O-V$;

B is $-C(Z)-$, $-Y-$ or a covalent bond;

D is $-S(O)_0$ or $-N(R_a)(R_i)$;

R₁ is ~~$-S(O)_2-CH_3$~~ or $-S(O)_2-NH_2$;

R₁' at each occurrence is independently a hydrogen, a halogen, a methyl or CH₂OH;

R₂ is a substituted lower alkyl group, a cycloalkyl group, an aryl group or a heterocyclic ring;

R_4 and R'_4 at each occurrence are independently a hydrogen, a halogen, a lower alkyl group or an alkoxy group; or R_4 and R'_4 taken together with the carbon atom to which they are attached are a substituted lower alkyl, a cycloalkyl group, an aryl group or a heterocyclic ring;

V is $-\text{NO}$, $-\text{NO}_2$, or a hydrogen; with the proviso that when V is hydrogen and R_5 is variable (a), then at least one of R_4 and R'_4 must be a halogen;

Y at each occurrence is independently an oxygen, $-\text{S}(\text{O})_o-$ or $-\text{N}(\text{R}_a)\text{R}_i-$;

Z is an oxo, a thial, an oxime or a hydrazone;

Q is Y or a covalent bond;

W at each occurrence is independently an aryl group, an alkylaryl group, a heterocyclic ring, or an alkylheterocyclic ring;

E is $-\text{C}(\text{O})$ or $-\text{S}(\text{O})_o$;

R_a is a lone pair of electron, a hydrogen, or a lower alkyl group;

R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyl, arylsulphonyloxy, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-(\text{C}(\text{R}_4)(\text{R}'_4))_n-\text{O}-\text{V}$, a bond to an adjacent atom creating a double bond to that atom, or $-(\text{N}_2\text{O}_2)^-\cdot\text{M}^+$, wherein M^+ is an organic or inorganic cation;

o is an integer from 0 to 2;

k is an integer from 1 to 6;

p at each occurrence is independently an integer from 0 to 10; and

n at each occurrence is independently an integer from 2 to 10.